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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,256	07/14/2003	Timo Kalevi Korpela	Korpela 1	6902

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EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/619,256	KORPELA ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-14 and 17* is/are pending in the application.

4a) Of the above claim(s) *9-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8 and 17* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present application has been transferred from former Examiner Khanna to the present Examiner.

It was previously indicated that claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. There is new rejection over claim 5 (35 USC 112 1st, Scope of Enablement). However, it is noted that the peptide sequence Thr-Ala-Thr-Val-Thr-Val (SEQ ID NO: 1), in claim 5, was not found to be reasonably taught or suggested by the prior art of record.

It is requested though, in claim 5, line 2, that the term "a" be deleted the term --the-- inserted, to properly identify the scope of that which the peptide consists of, namely, "the" sequence of SEQ ID NO: 1.

Claim Objections

Claim 17 is objected to because of the following informalities: duplicate term "the" between lines 1 and 2. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112 1st Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 5-8, and 17 are rejected under 35 U.S.C. 112, first paragraph, because the

specification, while being enabling for reducing the formation of said surface adhesive organelles, does not reasonably provide enablement for *preventing* the same (see new amendment in claim 1; arguably the same would apply to 'preventing' self-polymerization of equal peptide units, although the previous Examiner disposition may have been guided by reasons unbeknownst to this Examiner). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants have reasonably demonstrated/disclosed that certain peptide may be used for reducing the formation of said surface adhesive organelles. However, the claims also encompass using the claimed lipid modulating drug to prevent the same, which is clearly beyond the scope of the instantly disclosed/claimed invention. Please note that the term "prevent" is an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does the term "treat", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes) - including preventing such phenomenon as formation of said surface adhesive organelles (which clearly is not recognized in the medical art as being a totally preventable condition).

Accordingly, it would take undue experimentation without a reasonable expectation of success for one of skill in the art to make and/or use the claimed composition, which would function to prevent the formation of said surface adhesive organelles.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-2, 5-8, and 17 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained for the reasons of record. Applicant's arguments/amendments have been considered but are not found persuasive.

Applicant argues that removing the phrase "the structure of the" and leaving "An antimicrobial peptide corresponding to active sites of amino-terminal extension of subunits assembling surface adhesive organelles..." still fails to meet the requirements of 112 2nd, that the invention be 'distinctly claimed', in the eyes of Examiner. Namely, what active site/sites of said extensions are to correspond to the invention has contemplated? Additionally, the awkwardness of the claim language arguably renders the invention indefinite; namely "active sites of amino-terminal extension of subunits...". What subunits? Are these extension (singular) or extensions (plural) of said subunits? And what portion of these extension or extensions (e.g. what active site/sites therein; receptor binding)?

The rejection is repeated for continuity of record:

Claim 1 recites the limitation "corresponding to the structure of the active sites of the amino-terminal extension". It is not clear whether this limitation is intended to structurally limit the antimicrobial peptide by reciting its presence at the N-terminus or whether the intended structure of a sequence of the antimicrobial peptide is being correlated with the structure of the

active-site of an amino-terminal extension. Thus, claim 1 is indefinite. Claims 2-3, 5-8, 15-17 depend from claim 1, and therefore are indefinite.

Claim Rejections - 35 USC § 112 1st Written Description & Enablement

The rejections of claims 1-2, 6-8, and 17 under 112 1st paragraph, are maintained in their entirety. Applicant's arguments have been considered, but are not found persuasive. Applicant's only argument is that the peptide are of "short length" and thus pass muster under 112 1st. The length of the peptide is not the issue. Rather, the substantive issue is the lack of concreteness as to the structure within that length (where possession of which amino acid residues and where is described) or how to arrive at said length of peptide (e.g. why it would not require undue experimentation to determine the active sites of said gram-negative bacteria and those combinations that still function as an antimicrobial). Neither of which Applicant's arguments have addressed. This Examiner agrees with the previous Examiners analysis that the invention (product, peptide) as broadly claimed, lack sufficient structure, and/or function, or other evidence to satisfy the "possession" and "undue experimentation" litmus tests under both these prongs. Again the intended use of this product is not given patentable weight. Applicant has 5 sequences (SEQ ID NOS: 1-5) which appear to satisfy both prongs. Applicant may wish to consider amending the claims thereto, for which this Examiner is willing to extend the search & examination.

The rejections are both repeated for continuity of record:

Claims 1-2, 6-7, and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, claims 1-2, 6-7, and 15-17 recite an antimicrobial peptide or inhibitor with unknown sequence that correlates to a tertiary structure of an active site formed from the assembly of surface organelle and intended use only. As the genus of antimicrobial peptides, encompasses any random length, without any common sequence core, and with any secondary structure, as long as it corresponds to the tertiary structure of the active site formed from the assembly of surface organelle also with unknown structure, one skilled in the art would conclude that the disclosure of SE ID NO: 1, 4, and 5 is not representative of the undefined genus recited in the claims. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Therefore, the inventor, at the time the application was filed was not in possession of the broad genus comprising "antimicrobial peptides" or "inhibitors" needed to practice the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequence that is the same as in SEQ ID NO: 1, 4 and 5, the skilled artisan cannot envision the detailed structure of the claimed peptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Therefore, only the sequence that is the same as that of SEQ ID NO: 1, 4 and 5, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-2, 6-7, 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabling for using SEQ ID NO: 1, 4 and 5 for the in vivo use as antimicrobials, does not provide enablement for all in vivo uses for all undefined antimicrobial peptides that correspond to the tertiary structure of the active site formed from the assembly of surface organelle, also with unknown structure. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with claim 1.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. Neither undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Nature of the invention. The instant invention is to antimicrobial peptides that correspond to the structure of the active sites of amino-terminal extension of subunits, wherein the antimicrobial peptide is capable of preventing self-polymerization of equal peptide units.

Breadth of the claims. According to the language of the claims, the use of the antimicrobial peptide can be extrapolated to any and all peptides that correspond to the structure of the active site of the amino-terminal extension of subunits.

State and un/predictability of the prior art. The claimed subject matter is lacking in predictability. While examples in the art (WO 0032785) exist for the use of peptides that comprise the four consecutive amino acid sequence, TTKL, as in SEQ ID NO:4, the facts indicate that TTKL as disclosed in the reference encodes a helicase domain. Specifically, the state of the prior art as exemplified by Macino indicates that two oligopeptides, the instant and one taught by the reference, have different functions although they are capable of corresponding to the structure of the active sites of amino-terminal extensions.

Given that determining any and all uses of oligopeptides with similar sequences and intended structure correlation is empirical and unpredictable in nature, it flows logically that one would be unduly burdened with experimentation to determine any and all the pharmaceutical uses of all oligopeptides encompassed by the antimicrobial peptide, which would be impossible in many lifetimes.

Working examples. While the only working examples given in the specification are limited to the "use" of SEQ ID NO: 1,4 and 5 for antibacterials, there is no suggestion as to what the specific uses of any and all uses of other antimicrobial peptides is, given the only correlation with the intended tertiary structure of the active-site amino terminal extension.

Guidance in the specification. The specification provides little guidance regarding the use of utilizing sequences of random length further comprising at least four consecutive amino acids, as in SEQ ID NO: 4. There is a lack of predictability in the art regarding the in vivo use of pharmaceutical peptides for sequences with only an intended structure correlation.

Amount of experimentation necessary. Given the unpredictability of the art, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to make antimicrobial peptides with a tertiary structure correlation for any intended use. If undue experimentation is required to make antimicrobial peptides for any intended use, it would certainly require undue experimentation to determine the "use" of all antimicrobial peptides to determine which would be enabled for pharmaceutical use. This amount of experimentation would be impossible in many lifetimes.

Relative Skill of those skilled in the art. In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a Ph.D. with several years of experience in the art. As the cited art would point to, even with a level of skill in the art that is Ph.D. predictability of the results is not invariable.

In consideration of each of the factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual date to the contrary, the amount and level of experimentation needed is undue.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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